Site visit inspection report on compliance with HTA licensing standards

Astex Therapeutics Ltd

HTA licensing number 12122

Licensed under the Human Tissue Act 2004 for the

- **storage of relevant material which has come from a human body for use for a scheduled purpose**

05 July 2017

Summary of inspection findings

The HTA found the Designated Individual, the Licence Holder, the premises and the practices to be suitable in accordance with the requirements of the legislation.

Although the HTA found that Astex Therapeutics Ltd (the establishment) had met the majority of the HTA's standards, one minor shortfall was found in relation to risk assessments (standard GQ6(a)).

Particular examples of strengths and good practice are included in the concluding comments section of the report.

The HTA's regulatory requirements

Prior to the grant of a licence, the HTA must assure itself that the Designated Individual (DI) is a suitable person to supervise the activity authorised by the licence and that the premises are suitable for the activity.

The statutory duties of the Designated Individual are set down in Section 18 of the Human Tissue Act 2004 (HT Act). They are to secure that:

- the other persons to whom the licence applies are suitable persons to participate in the carrying-on of the licensed activity;
- suitable practices are used in the course of carrying on that activity; and
- the conditions of the licence are complied with.

Its programme of site visit inspections to assess compliance with HTA licensing standards is one of the assurance mechanisms used by the HTA.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. They are grouped under four headings:

- consent
- governance and quality systems
- traceability
- premises facilities and equipment.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that there has been a shortfall against a standard, the level of the shortfall is classified as 'Critical', 'Major' or 'Minor' (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is provided.

HTA inspection reports are published on the HTA's website.

Background to the establishment

Astex Therapeutics Ltd is part of an international pharmaceutical company. The company's activities in the UK focus on preclinical research and development. The establishment uses human tissue samples with the aim of developing and characterising small molecule drugs.

The establishment is licensed by the HTA under the HT Act for the storage of relevant material which has come from a human body for use for a scheduled purpose. The establishment stores human samples for use for the scheduled purpose of 'research in connection with disorders, or functioning, of the human body'.

The establishment has been licensed by the HTA since July 2007. The establishment was last inspected by the HTA in May 2011. This report describes the second routine inspection of the establishment. Since the last inspection, the establishment has increased its use of human tissue and implemented new quality management procedures. In May 2017, the licence was extended to include an additional building on the same licensed premises.

Samples include cell pellets, buccal swab samples and tissue samples on blocks and microscope slides. The majority of samples stored under the licence are acquired from commercial, third party organisations. The establishment also receives some human samples from academic organisations. The establishment also stores samples as part of approved clinical trials; some of these samples fall under the requirements of the HT Act by virtue of being covered only by overseas clinical trials approval (refer to Advice, item 3).

The establishment requires that researchers obtain approval from the DI to acquire human samples for storage and use at the establishment. The approval process includes checks on the documentation and consent statements from the third party organisations supplying samples to provide assurance that consent has been sought in accordance with the regulatory requirements (refer to Advice, item 1). The approval process is documented and a centralised record is kept of collections of samples stored under the HTA licence.

At the time of the inspection, the establishment was storing a collection of fixed tissue samples blocks and tissue samples on microscope slides at room temperature. These samples are stored in a secure laboratory. The establishment was also storing frozen tissue samples and cells in -80°C or -150°C freezers, and a collection of samples on microscope slides in one -20°C freezer (refer to Advice, item 9). The freezers are secured and located in secure laboratory areas. The establishment uses an automated alarm system to alert staff of deviations from the set acceptable temperature ranges, including a call-out notification procedure. The establishment has contingency arrangements for on-site and off-site temperature-controlled storage.

The DI and Persons Designated (PDs) maintain oversight of samples stored under the licence. All human samples are anonymised prior to being transported to the establishment. Samples are assigned a unique identification code, which is used to track sample receipt, storage, use and disposal (see Advice, item 8). The establishment uses electronic databases to provide traceability of samples. The establishment also uses paper forms to record details of sample receipt, use and disposal. Completed forms are stored in secured fire-proof filing cabinets. The establishment plans to implement an electronic Laboratory Information Management System (LIMS) for tracking samples, in the near future.

Description of inspection activities undertaken

The inspection timetable was developed in consideration of the activities conducted under the licence, compliance update information, the findings of the previous inspection and discussions with the DI. The inspection included: review of the establishment's procedures for conducting activities under the licence; interviews with staff; visual inspection of the areas where samples are stored under the licence; and audits of sample traceability.

At the time of the inspection, the establishment was setting up new temperature-controlled storage facilities. These facilities were included in the visual inspection.

Audits of sample traceability were conducted of samples from each collection stored under the licence and included:

- 15 frozen tissue or cell samples from sample to record and nine frozen tissue or cell samples from record to sample;
- 21 frozen slides from sample to record and 21 frozen slides from record to sample; and
- Two blocks and six slides from sample to record and ten slides from record to sample in room temperature storage.

There were no discrepancies in the traceability of these samples. Some samples were labelled with the batch code or supplier's catalogue code and not the unique identification code; however, the establishment was able to demonstrate traceability of these samples by accurate records of numbers of samples within the batches (see Advice, item 8). The establishment plans to affix additional labels, which will include the unique identification code, to these samples when they implement the electronic LIMS.

The establishment was storing 23 microscope slides containing hair follicles. Although the establishment was not aware that these samples are relevant material and so subject to the requirements of the HT Act, they demonstrated full traceability of these samples (see Advice, item 7).

Audits were also undertaken of sample receipt, including assurance of consent, and sample disposal; no discrepancies in these records were found.

Inspection findings

The HTA found the Licence Holder, the Designated Individual and the premises to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored		
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and HTA's Codes of Practice	Although the establishment has risk assessments relating to health and safety risks of working with human samples and failure of storage facilities, there are no documented risks assessments of the regulatory risks associated with the storage of human tissues for use in research. *Refer to Advice, item 6.*	**Minor**

Advice

The HTA advises the DI to consider the following to further improve practices:

No.	Standard	Advice
1.	C1(c)	The DI is advised to consider documenting a checklist of the checks performed on the consent status of samples as part of the establishment's procedure to approve samples being obtained to be stored under the licence. This will help to ensure that the approval process is conducted in a consistent manner and will provide further assurance that all consent has been given in accordance with the regulatory requirements for all samples stored under the licence. The DI is advised to ensure that any restrictions on the consent for the use of samples are detailed on the sample traceability databases. This will help to ensure that samples are stored and used in accordance with the consent given.
2.	GQ1(a)	The establishment has a 'HTA Policy' document which sets out the policies and procedures relating to samples stored under the licence. The DI is advised to review this document to ensure that it provides sufficient details of procedures. This will help to ensure that procedures are conducted in a consistent manner and in accordance with the HT Act and the HTA's Codes of Practice. *See also Advice, items 3 and 5.*

3.	GQ1(a)	The DI is advised that the exception set out in the HT Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006 which allows human tissue held for a specific research project to be stored on premises without a HTA licence only applies where the project has been approved by a recognised research ethics committee (REC). This can be either: a) a REC recognised or established by, or on behalf of, the HRA under the Care Act 2014 or any other group of persons which assesses the ethics of research involving individuals and which is recognised for that purpose by, or on behalf of, the Welsh Ministers or the Department of Health in Northern Ireland; or b) an ethics committee recognised by United Kingdom Ethics Committee Authority (UKECA) to review clinical trials of investigational medicinal products under the Medicines for Human Use (Clinical Trials) Regulations 2004. Clinical trials approval from an ethics committee overseas, and not recognised by UKECA, does not provide an exemption from the licensing requirements of the HT Act. Further information on the licensing requirements in this regard can be found in the HTA's Code of Practice E (paragraphs 86 – 90 and 124 – 125): www.hta.gov.uk/sites/default/files/Code%20E%20-%20Research%20Final_0.pdf The DI is advised to include details of the licensing requirements and the definition of a 'recognised REC' in the establishment's 'HTA Policy' document. This will help to raise awareness of the licensing requirements of the HT Act and ensure that these samples are included in the DI's oversight of the licence.
4.	GQ2(a)	The establishment has recently introduced a schedule of audits specifically relating to governance of the HTA licence and samples stored under the licence. The DI is advised to ensure that audits of licensed activities continue to be scheduled and undertaken. The DI is advised that the HTA licensing standards for this sector do not require that these audits are conducted by an independent, external auditor.
5.	GQ5(a)	The DI is advised to include further information about the establishment's procedures for reporting adverse events in its 'HTA Policy' document, including details of the types of events that should be reported via the establishment's internal procedures. Examples of adverse events include, but are not limited to: • consent not sought in accordance with the HT Act requirements; • sample used not in line with consent given; • specimen loss; • missing or incorrect documentation; • security breach; • abnormalities in storage temperature; and • incorrect or inappropriate disposal.

6.	GQ6(a)	DI should ensure that documented risk assessments cover all of the practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. In addition to the risks covered by the establishment's risk assessments, the DI should ensure that the following risks have also been assessed: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; • loss of human tissue; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment; and • incorrect disposal. Further guidance on risk assessments of activities conducted under the HTA licence can be found in the HTA's research sector licensing standards and guidance document on the HTA website: www.hta.gov.uk/sites/default/files/Code%20E%20Research%20Standards%20and%20Guidance.pdf.
7.	T1(a)	The DI is advised that hair follicles are relevant material and are subject to the licensing and consent requirements of the HT Act. The DI is advised to ensure that the hair follicle samples stored at the establishment are subject to the establishment's governance procedures for the licence and that the traceability records for these samples are recorded on their traceability databases.
8.	T1(a)	The DI is advised to ensure that all samples are labelled with a unique identification code. Although samples are assigned a unique identification code, some samples are not labelled with this code and are tracked in storage using the batch code or the supplier's catalogue code. The establishment plans to affix additional labels, which will include the unique identification code, to these samples when they implement the electronic LIMS. This will help to ensure that sample traceability is maintained where there are multiple samples in a batch. This may become more important to help to ensure traceability of samples is maintained in the event that more samples are stored at the establishment and if samples are used more frequently.
9.	T1(c)	The DI is advised to consider labelling storage units to indicate that they contain human samples stored under the licence and with the storage unit identification number. This will help to ensure that sample traceability records accurately reflect storage locations and that human and non-human samples are stored separately. Where human and non-human samples are stored in the same storage unit, the DI is advised to use separate storage boxes or compartments to separate these samples.
10.	N/A	A copy of the licence is displayed in the buildings' central entrance areas. The DI is asked to display a copy of the HTA licence in all areas where samples are being stored under the licence. This will help to raise awareness that samples are being stored under the licence.

Concluding comments

This report outlines the second, routine HTA site visit inspection of Astex Therapeutics Ltd. Although one minor shortfall was identified, a number of strengths and areas of good practice were observed during the inspection, including:

- Staff at the establishment have clearly defined roles for sample management including procurement, receipt, storage and use of samples. Staff have received training in the HT Act requirements and the establishment's procedures specific to their roles working with samples under the licence; this includes staff responsible for receiving deliveries of human samples. The DI has also nominated PDs, who undertake key activities under the licence and help to oversee storage of samples in the two buildings. There appeared to be good communication between staff in the departments involved in the inspection.

- Staff demonstrated a commitment to compliance with the HTA's licensing standards and that they strive towards continual improvement of practices. Staff were open to the advice offered by the HTA during the inspection.

- The establishment has undertaken a full audit of their procedures for governance of the licence and the storage of samples under the licence using an external auditor.

- The establishment is undertaking validation of temperature-controlled storage facilities and alarming arrangements as part of the process of setting up new temperature-controlled storage facilities.

The HTA requires the Designated Individual to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfall will be addressed, within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

The HTA has assessed the establishment as suitable to be licensed for the activities specified subject to corrective and preventative actions being implemented to meet the shortfall identified during the inspection.

Report sent to DI for factual accuracy: 18 July 2017

Report returned from DI: 26 July 2017

Final report issued: 28 July 2017

Completion of corrective and preventative actions (CAPA) plan

Based on information provided, the HTA is satisfied that the establishment has completed the agreed actions in the CAPA plan and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 26 March 2018

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below; those not assessed during the inspection are shown in grey text. Individual standards which are not applicable to this establishment have been excluded.

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities. b) There is a document control system. c) There are change control mechanisms for the implementation of new operational procedures. d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff. e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities. b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training. b) There are documented induction training programmes for new staff. c) Training provisions include those for visiting staff.

d) Staff have appraisals and personal development plans.
GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records. b) There are provisions for back-up / recovery in the event of loss of records. c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).
GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems. b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. b) Risk assessments are reviewed regularly. c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it. b) A register of donated material, and the associated products where relevant, is maintained. c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom. d) A system is in place to ensure that traceability of relevant material is maintained during transport. e) Records of transportation and delivery are kept.
T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice. b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment standards
PFE1 The premises are secure and fit for purpose
a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose. b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained. c) There are documented cleaning and decontamination procedures.
PFE2 There are appropriate facilities for the storage of bodies and human tissue
a) There is sufficient storage capacity. b) Where relevant, storage arrangements ensure the dignity of the deceased. c) Storage conditions are monitored, recorded and acted on when required. d) There are documented contingency plans in place in case of failure in storage area.
PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored
a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept. b) Users have access to instructions for equipment and are aware of how to report an equipment problem. c) Staff are provided with suitable personal protective equipment.

Appendix 2: Classification of the level of shortfall

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the HT Act or associated Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant risk to human safety and/or dignity or is a breach of the Human Tissue Act 2004 (HT Act) or associated Directions

   or

   A combination of several major shortfalls, none of which is critical on its own, but which together could constitute a critical shortfall and should be explained and reported as such.

   A critical shortfall may result in one or more of the following:

   (1) A notice of proposal being issued to revoke the licence

   (2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

   (5) Directions being issued requiring specific action to be taken straightaway

2. **Major shortfall:**

   A non-critical shortfall that:

   - poses a risk to human safety and/or dignity, or
   - indicates a failure to carry out satisfactory procedures, or
   - indicates a breach of the relevant CoPs, the HT Act and other relevant professional and statutory guidelines, or
   - has the potential to become a critical shortfall unless addressed

   or

   A combination of several minor shortfalls, none of which is major on its own, but which, together, could constitute a major shortfall and should be explained and reported as such.

   In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major, but which indicates a departure from expected standards.

   This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based or site visit.

   In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

After an assessment of your proposed action plan you will be notified of the follow-up approach the HTA will take.